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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,140	01/22/2004	Hing C. Wong	TNA-005.05	6085

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EXAMINER	
BORGEEST, CHRISTINA M	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/764,140	WONG ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 July 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37,39-42 and 47-55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37, 39-42 and 47-55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12 July 2007 has been entered. Claims 37, 39-42 and 47-55 are under examination.

Objections/Rejections Maintained/New Rejection

Priority

The issue raised by the Examiner in the Office action mailed 16 May 2006 (and the subsequent Office actions mailed 12 March 2007 and 3 August 2007) regarding Applicants' non-compliance with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) because the disclosure of the prior-filed application, Application No. 10/293,417, (and its parent applications, now U.S. Patents 6,555,319 and 5,986,065) fail to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application (the '417 application does not provide enablement or written description for ***treatment of sepsis*** with the claimed antibodies) thus making the effective filing date for the application 22 January 2004, is maintained.

Applicants offer the following arguments at p. 4, last paragraph through p. 5, 1st paragraph:

1. A skilled artisan at the time that the '806 application (aka '065 patent) was filed would have known that sepsis could be treated by addressing the resulting disseminated intravascular coagulation phenotype. For example, it was known from Levi et al. 1994 (document number EO from the IDS filed on January 19, 2006) that "endotoxin-induced activation of coagulation appears to be mediated by the tissue factor-dependent pathway."

This argument has been fully considered but is not found persuasive for the following reason. Levi et al. is not incorporated by reference in the '065 patent, so their teachings are not part of the disclosure of the '065 patent.

2. The '806 specification (or '065 patent) teaches that antibodies of the invention could be used to detect native human tissue factor in a biological sample, such as that from a patient suffering from septic shock (Column 12, lines 19-38), and that antibodies of the invention could then be administered to a primate, such as a human, to prevent or reduce thromboses (Column 9, lines 63-65) as are manifested during sepsis. Moreover, the '806 specification teaches therapeutic compositions (Column 9, line 66 to Column 10, line 22), methods of administration (Column 10, lines 32-39), and therapeutic dosages (Column 10, lines 39-62) relevant to the treatment of sepsis.

This argument has been fully considered but is not found persuasive for the following reason. First, the citation from the '065 patent at column 12, lines 19-38 actually says the antibodies could be used to ***detect*** native human TF in a biological sample, and that the samples could be taken from mammals suffering a long list of other disorders, of which septic shock syndrome (which is a complication following sepsis) is one. See the excerpt from column 12, lines 19-38:

> As also discussed above, antibodies of the invention can be employed to detect native human TF in a biological sample, particularly native TF associated with a blood clot. Exemplary biological samples include blood plasma, serum, saliva, urine, stool, vaginal secretions, bile, lymph, ocular

> humors, cerebrospinal fluid, cell culture media, and tissue, particularly vascular tissues such as cardiac tissue. Samples may be suitably obtained from a mammal suffering from or suspected of suffering from a thrombosis, preferably restenosis, associated with, e.g., an invasive medical procedure such as cardiopulmonary bypass surgery; a heart ailment such as myocardial infarction, cardiomyopathy, valvular heart disease, unstable angina, or artrial fibrillation associated with embolization; a coagulopathy including disseminated intravascular coagulation, deployment of an implementation such as a stent or catheter; shock (e.g., septic shock syndrome), vascular trauma, liver disease, heat stroke, malignancies (e.g., pancreatic, ovarian, or small lung cell carcinoma), lupus, eclampsia, perivascular occlusive disease, and renal disease.

The claims are drawn to treatment of sepsis, so detection of TF in biological samples from patients suffering from a long list of diseases is not sufficiently enabling for the currently recited claims. In other words, Applicants would need to explain how detection of native human TF in a biological sample translates into therapy for sepsis. Furthermore, the citation of the '065 patent at column 9, lines 63-65 make no mention of sepsis, but rather only says "to reduce thrombosis such as restenosis." In addition, the other citations of the '065 patent do not provide any support for treatment of sepsis in particular.

3. The specification provides a literal basis for the term "septic shock syndrome" at page 6, first paragraph.

This argument has been fully considered but is not found persuasive for the following reason. The instant specification at p. 6 1st paragraph does not define sepsis, and furthermore, a definition of sepsis cannot be found anywhere in the instant application, though the same paragraph recited above from column 12, lines 19-38 of the '065 patent can be found at paragraph [0071] of the instant application. As

indicated in the Advisory action mailed 3 August 2007 (along with the provision of the cited reference), a definition of sepsis can be found on Medline at: nlm.nih.govlmedlineplusencylarticlelOOO666.htm. Since the instant claims are drawn to treatment of sepsis and not merely detection of TF, Applicants arguments that the '065 patent provides enablement and written description are not found persuasive. The earlier filed applications do not contain any evidence that there was a conception of treatment of sepsis with the claimed methods. In other words, while the earlier applications disclose diagnosis of septic shock syndrome with the recited antibodies, it does not disclose treatment either ipsis verbis or by natural flow from the specification. Finally, an evaluation of working examples in the prior filed applications are not commensurate in scope with treatment of septic shock syndrome. Absent persuasive evidence to the contrary, the prior filed applications cannot provide enablement or written description for the instantly claimed methods, and the effective filing date for the instantly claimed method is 22 January 2004.

Claim Rejections - 35 USC § 112, first paragraph

Claim Rejections - 35 USC § 112, first paragraph – Written Description

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 37, 39-42, 47-55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject

matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a partial structure in the form of "fragment thereof". There is not even identification of any particular portion or fragment of SEQ ID NO: 4 that must be conserved. Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of SEQ ID NO: 4 ***or an antigen binding fragment thereof*** (as taught, for instance, at paragraph [0060] of the instant specification) the skilled artisan cannot envision the detailed chemical structure of the encompassed

polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO: 4 or an antigen binding fragment thereof, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 37-42, 44, 47-55 under 35 U.S.C. 103(a) as being obvious over Wong et al. (WO 98/40408, published 17 September 1998) in view of Taylor (Crit Care Med. 2001, 29(7 Suppl): S78-89) as set forth at pages 8-11 in the in the previous Office action mailed 16 May 2006 is maintained for reasons of record and the following.

Applicants argue at p. 6, 1st full paragraph, that the Wong et al. is not available as prior art because it was published after 10 March 1997, to which the instant application claims benefit.

This argument has been fully considered but is not found persuasive, because as noted in the section under Priority, unless the Applicants can perfect the claim to benefit under 35 U.S.C. 119 (e), because the prior applications did not set forth that treatment was considered part of the invention, the effective filing date has been determined to be 22 January 2004.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent

and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 37, 38, 40, 41, 42, 47, 48, 49, 50 and 51 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 32, 34, 35, 38, 46, 47 and 48 of copending Application No. 10/310,113 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claims 37, 38, 39, 40, 41, 42, 44, 47, 50 51, 52, 53 and 54 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 37, 38, 39, 40, 41, 42, 43, 44, 45, 48, 53, 54, 55 and 57 of copending Application No. 10/618,338 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claim 37 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 25, 26, 27 and 33 of copending Application No. 11/087,528 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

The provisional rejection of claims 37, 47, 49, 50 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 66 of copending Application No. 11/122,622 in view of Taylor (cited in previous Office action mailed 16 May 2006) is maintained for reasons of record.

Applicants' indication of a willingness to file a terminal with respect to the above listed co-pending applications at p. 6, last paragraph of their response filed 12 July 2007 is noted. In the meantime, the provisional rejections are maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00am - 2:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on 571-272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christina Borgeest, Ph.D.

/Elizabeth C. Kemmerer/
Primary Examiner, Art Unit 1646